REMARKS

The applicants appreciate the Examiner's thorough examination of the application and request reexamination and reconsideration of the application in view of the preceding amendments and the following remarks.

REJECTIONS UNDER 35 U.S.C. §112, 2ND PARAGRAPH

The Examiner rejects claims 2, 8, 10, 14, 15 and 24 under 35 U.S.C. §112, second paragraph.

Particularly, the Examiner states that with respect to claims 2, 10 and 15, the specification allegedly does not reasonably apprise one of ordinary skill in the art as to the meaning of "high", quoting MPEP §2173.05(b).

The applicants respectfully submit that the recitation of the element "high" is not indefinite according to MPEP §2173.05(b). According to MPEP §2173.05(b) (with emphasis added):

> The fact that claim language, including terms of degree, may not be precise, does *not* automatically render the claim indefinite under 35 U.S.C. 112, second paragraph ... *Acceptability of the claim language depends on whether one of ordinary skill in the art would understand what is claimed, in light of the specification.*

The meaning of a high concentration of contrast agent is well known to those skilled in the art. Moreover, the meaning of a high concentration of contrast agent in a patient's blood is discussed exhaustively throughout the applicants' specification. See e.g. the applicant's specification, for example as follows:

[0012] ... Multiple studies have established a correlation between the extent of kidney damage caused by contrast injections and the amount of contrast administered during the intervention ...

[0020] During a medical intervention ... contrast is given in a series of bolus injections ...the contrast concentration in blood increases with each injection ... As a result, the concentration of contrast in blood keeps increasing and can peak at dangerously high levels, well outside of its therapeutic window ...

[0021] ... kidneys are exposed to relatively high concentration of contrast in blood during the time window that corresponds to the peak concentration of contrast ...

[0026] It is established that the high concentration duration (also called time period or time window) can last up to several hours until the contrast is sufficiently redistributed into the total body extracellular blood volume ... Accordingly, after the redistribution, the concentration of the contrast agent in the blood is 10 times lower and significantly less hazardous to the kidney ...

[0056] Figure 6 is a graph that illustrates the changes in the blood during and after an interventional procedure ... The first injection of contrast is given to the patient at the point 401 at the beginning of the procedure. The concentration curve starts to rise quickly. ... The contrast injections are stopped at a point 402 ... The concentration of contrast reached its peak at this point ...

[0057] After the contrast concentration has reached its peak 402 and the injections of additional contrast stop, the concentration curve enters into the rapid decline segment between points 402 and 403 ... After the redistribution phase 402 to 404 is complete, the contrast concentration in blood is reduced much slower. During this phase, the kidneys alone clear the contrast from the blood ...

[0058] The method and system disclosed herein protects at least one kidney of the patient from the exposure to high concentration of contrast in blood. This protection is implemented during the rise phase of the contrast-concentration time curve 401 to 402, peak phase (around point 402) and the redistribution phase (403 to 404).

The applicants submit that those of ordinary skill in the art would understand what is claimed, in light of the specification. MPEP §2173.05(b).

Those skilled in the art also understand that a high concentration may vary from patient to patient. See e.g. paragraph [0023]. Nonetheless, the meaning of a high concentration – with respect to a particular patient – does not change, and is still readily understood by those skilled in the art.

Additionally, the term "high concentration" is sufficiently accurate in view of the subject matter. See e.g. MPEP 2173.05(b), quoting Orthokinetics, Inc. v. Safety Travel Chairs, Inc. In that case, the subject claim defined a wheelchair "so dimensioned as to be insertable through the space between the door frame of an automobile and one of the seats". In holding that the claim was definite, the court noted that the patent law does not require that all possible lengths corresponding to the spaces of hundreds of different automobiles be listed in the patent, let alone that they be listed in the claims.

Likewise here, the applicants submit that patent law does not require recitation of all possible high concentrations for a variety of patients and factors. Nonetheless, the applicants have provided an example of a range of concentrations in the specification. See e.g. paragraph [0056], lines 18-21.

Accordingly, the applicants respectfully request that the Examiner withdraw the 35 U.S.C. §112, 2nd paragraph rejections based on the recitation of a "high" concentration, currently recited claims 1, 10, and 14.

With respect to claim 8, the Examiner states that there is lack of antecedent basis. In response, the applicant has amended claim 8 to change its dependency.

With respect to claim 14, the Examiner states that it is unclear if the step of injecting contrast is positively recited in view of claim 23.

Claim 14 recites "elevating a renal vein blood pressure during a period coinciding with an injection of contrast in blood of the patient". Thus, this element of claim 14 defines *when* renal vein blood pressure is elevated (i.e. during a period coinciding with an injection of contrast in blood of the patient). Claim 23 recites the step of *injecting* the contrast agent into a blood vessel of the patient.

The applicant therefore respectfully submits that claim 14 is not unclear.

With respect to claim 24, the Examiner states:

> Claim[] 24 is indefinite because "the period of contrast" is defined as from injection until a 50% reduction of contrast (claim 24). However, a period of contrast would readily be understood to include a period in which contrast is present (i.e. 40% or 25% of injection concentration).

Dependent claim 14 recites a period when renal vein blood pressure is elevated (i.e. during a period coinciding with an injection of contrast in blood of the patient).

Claim 24 essentially defines one such period, i.e. from injection until there is a fifty percent reduction in the concentration of the contrast in the blood from a peak concentration. Thus, if there is (only) a 25% reduction, or a 40% reduction, the step of elevating the renal vein blood pressure will be maintained, because there has not yet been a 50% reduction. This does not make the claim indefinite.

On the contrary, it defines one time period during which elevation of renal blood pressure will be maintained. The boundaries of the claim(s) are readily discernible. See e.g. MPEP §2173.05(c) I.

Accordingly, the applicants request that the Examiner withdraw the rejection of the claims which are based on 35 U.S.C. §112, 2nd paragraph.

REJECTIONS UNDER 35 U.S.C. §102(b)

As a preliminary matter, neither *Doty et al.* nor *Sterman et al.*, each discussed in more detail below, suggest in any way a solution for preventing kidney damage caused by contrast agents. In contrast to these cited references, the applicants herein recognized an unsolved problem, and provided a solution, which is the subject of the applicants' claims. The solution was counterintuitive. See e.g. the applicants' specification at paragraph [0030].

The applicants recognized that renal dysfunction is associated with the use of radiographic contrast media, and recognized the need to reduce the incidence and severity of contrast associated nephropathy. See e.g. applicants' specification at page 5, lines 8-10 and page 7, lines 17-19.

The applicants also recognized that contrast agents affect the target organ in proportion to the concentration of active chemical agent in blood plasma that flows through the organ – e.g. a kidney – and the duration of exposure. Kidneys are damaged primarily by exposure to high concentrations of contrast in blood. See e.g. applicants' specification at page 9, lines 17-23 and page 13, lines 4-5.

The applicants further recognized that elevated renal vein pressure often exhibits diminished renal function and reduced renal blood flow, that such diminished renal function and reduced venal blood flow would be beneficial to protect the kidney(s) during times of peak exposure to a contrast agent, and that one way to effect elevated renal vein pressure is by creating a removable obstruction of the renal vein. See e.g. the applicants' specification at page 17, lines 10-27 and at page 18, lines 1-4.

These concepts and more are more fully set forth in the applicants' specification.

In summary, in accordance with embodiments of the subject invention, the applicants have claimed novel, inventive, and non-obvious methods protecting at least one kidney.

Doty et al.

The Examiner rejects claims 1-5, 8-12, 14, 16-19, 22 and 25-26 under U.S.C. §102(b) as being anticipated by *Doty et al.*, Effect of Increased Renal Venous Pressure on Renal Function.

In contrast to the applicants' independent claims 1 and 14 as amended, *Doty et al.* fails to disclose or teach a method for protecting a kidney; or protecting a kidney from insult caused by the presence of a contrast agent in the blood of a patient; or partially occluding at least one renal vein of the patient as part of a method for doing so; or *elevating a renal vein blood pressure during a period of high concentration of the contrast agent in the patient's blood*; or then reducing the renal vein blood pressure from the elevated blood pressure as part of the method.

In order to find anticipation, all of the elements of all of the claims be found within a single prior art reference. Also, "[t]here must be no difference between the claimed invention and the reference disclosure, as viewed by a person of ordinary skill in the field of the invention". See e.g. Scripps Clinic v. Genentech, Inc., 927 F.2d 1565, 18 USPQ 2d 1001, 1010 (Fed. Cir. 1991). Moreover, the applicants' claimed invention as a whole must be considered. See MPEP §2141.02.

At best, *Doty et al.* made an observation, namely, that increased renal vein pressure leads to decreased artery blood flow (and its typically damaging effects). The applicants took the inventive and counterintuitive/non-obvious step to use *Doty et al.*'s observations (regarding typically damaging effects of increased renal vein pressure) to provide a solution to a pressing, unsolved problem – protecting a kidney from contrast nephropathy.

In summary, *Doty et al.* fails to disclose the elements of the applicant's claimed method of protecting a kidney and/or minimizing radiocontrast nephropathy, including the failure to disclose the applicants' recitation of elevating a renal vein blood pressure during a period of high concentration of contrast agent in the patient's blood. *Doty et al.* further fails to disclose the applicants' claimed purpose for the method or the claimed function.

Accordingly, the applicants' claims are not anticipated by *Doty et al.*, and are in condition for allowance.

U.S. Pat. No. 6,599,231 to *Sterman et al.*

The Examiner rejects claims 1-6, 8, 9, 10, 14-20, 22 and 24 under U.S.C. §102(b) as being anticipated by U.S. Pat. No. 6,699,231 to *Sterman et al.*

In contrast to the applicant's claims, *Sterman et al.* does not disclose a method of protecting a kidney from insult by reducing renal functions of the kidney by increasing renal pressure in the renal vein.

Instead, *Sterman et al.* discloses quite the opposite. *Sterman et al.* does not protect the tissue. Instead, *Sterman et al.* discloses isolating the tissue (a kidney in one example) to protect the body from systemic toxicity. See e.g. *Sterman et al.* at column 1, lines 14-17; column 2, lines 31-35; column 16, lines 11-16; column 22, lines 62-63.

Additionally, *Sterman et al.* teaches fully occluding the arteries to block all blood flow, in order to protect the rest of the body or bodily system.

In contrast, the applicants claims (as amended for clarification) recite partially occluding at least one renal vein of the patient. See also e.g. applicants specification at paragraph [0031].

Moreover, the inhibition of renal function which would result from the applicants' claimed invention is not suggested by *Sterman et al.* See also applicants' dependent claim 2.

Instead, *Sterman et al.* discloses maintaining normality of the subject organ by profusing the organ using a lumen of the occluding catheter. In one such example, *Sterman et al.* teaches an excorporeal circulation system. See e.g. *Sterman et al.* column 14, lines 50-57; column 15, lines 20-25.

In summary, *Sterman et al.* fails to disclose the elements of the applicant's claimed method, nor its purpose nor its function.

Accordingly, the applicants' claims are not anticipated by *Sterman et al.*, and are in condition for allowance.

The Examiner also rejects claims 7, 13, 21 and 27 under 35 U.S.C. §103(a) as being unpatentable over *Sterman et al.* Claims 7, 13, 21 and 27 depend directly or indirectly from either independent claim 1 or independent claim 14, which are allowable for the foregoing reasons. Accordingly, claims 7, 13, 21 and 27 are also allowable for at least the same reasons.

CONCLUSION

The applicants submit that claims 1, 3-14, and 16-27 are in condition for allowance.

Each of the Examiner's rejections has been addressed or traversed. Accordingly, it is respectfully submitted that the application is in condition for allowance. Early and favorable action is respectfully requested.

If for any reason this Response is found to be incomplete, or if at any time it appears that a telephone conference with counsel would help advance prosecution, please telephone the undersigned or his associates, collect in Waltham, Massachusetts at (781) 890-5678.

Respectfully submitted,

Thomas E. Thompkins, Jr.
Reg. No. 47,136